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Pericentromeric transposition and shuffling of Xq28 loci identify an unusual aspect of chromosome structure and a novel mechanism for human genome plasticity. Evan E. Eichler[1], Laurie Gordon[1], Marcia Budarf[2], Norman Doggett[3], Richard Gibbs[4], David L. Nelson[4] and Harvey Mohrenweiser[1]. 1Human Genome Center, Lawrence Livermore National Lab.; 2Children's Hospital of Philadelphia, University of Pennsylvania; 3Center for Genome Studies, Los Alamos National Lab.; 4Human Genome Center, Baylor College of Medicine.

We have identified a 50 kb gene-rich region of Xq28 which has undergone recent and independent duplications to specific pericentromeric regions of autosomes. Two cassette units have been involved in these replicative transposition events: a 26.5 kb segment including the Xq28 creatine transporter and CDM genes, and a 9.5 kb segment incorporating the distal portion of the adrenoleukodystrophy locus. STS mapping and FISH analysis have localized the autosomal paralogous copies of these genes to 2p11.1/11.2, 10p11.1/11.2, 16p11.1/11.2 and 22q11.1/11.2, indicating an unusual propensity for these regions of Xq28 to duplicate to the heterochromatin/euchromatin boundary of pericentromeric regions. Large-scale comparative sequence analyses reveal nucleotide similaritities ranging from 92 to 98% among the duplicated genes and gene segments. Thus, the transposition events have occurred in recent evolutionary time (<5 mya). Comparative FISH analysis reveal both quantitative and qualitative differences in these duplication events among human, gorilla and chimpanzee chromosomes. Analysis of sequence located at the breakpoints of these duplicons has identified unusual CAAAAAG and CAGGG repeat structures. These repeat sequences appear to be absent among non-primates and are in humans organized in discrete blocks. The sequence and location of these repeats indicate that they are critical in the process of transposition integration. Preliminary analysis of 16p11.1/11.2 region has identified several transposed seqments from chromosomes other than Xq28. The distribution and dispersal of these duplicons identifies an unprecedented mechanism for targeted transposition which may have important implications in chromosome structure, genetic disease and genome evolution.

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